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ON THE FORM AND STRENGTH OF TREES: PART III. THE SECONDARY BRANCHES AND THEIR RELATION TO THE PRIMARY BRANCHES

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The secondary branches are considered in this note mainly for the purpose of applying the principle of maximum strength to the primary branches

1. A reason for secondary branches. If the secondary branches are treated as horizontal cantilevers, they may be subjected to the same mathematical analysis that was carried out previously (Opatowski, 1944b) for the primary branches. The same function K represents here the advantage in mechanical strength of a primary branch with many secondary branches with respect to a biologically equivalent primary branch with only one secondary branch.

2. A branch of maximum strength. The principle of maximum strength, which was applied to the trunk, (Opatowski, 1944a) may be used in a similar manner for the primary branches. It must be supplemented by the condition of maximum length of the branch, in the same way as in the case of the trunk the condition of maximum height had to be added to obtain the shape of the trunk. The conditions of maximum height for the trunk, and of maximum length for the branch, may both be justified by biological considerations.

We consider the primary branch as a horizontal cantilever which is bent under the action of its own weight and of the load due to secondary branches. We apply the ordinary methods of the theory of strength of materials. Since we do not discuss the growth of the branch, we may consider its weight as a fixed and known quantity. Then the conditions of maximum strength and of maximum length require that the maximum bending stress of each cross-section be the same throughout the cantilever, that is, that the latter be of *uniform strength* (see for instance, Timoshenko, 1940, pp. 209-210).

One may think to take into account the weight of the secondary branches by a suitable increase of the specific weight of the primary branch. However, the ordinary theory of strength of materials would be in such case inadequate to deal with the problem of uniform

strength, because it would lead to the inacceptable conclusion that the deflection at the free end of the branch is either imaginary or is infinity (Opatowski, 1945). Therefore, the secondary branches must be considered as concentrated weights. A similar situation arose in discussing a trunk of maximum strength (Opatowski, 1944a).

Let us number the secondary branches progressively: 1, 2, $\cdots$, i, $\cdots$, n, starting from the free end. Assume that the cross-section of the primary branch is circular and that the action of each secondary branch is equivalent to a concentrated weight B''_i acting at a certain point P_i. Let B'_i be the weight of that part of the primary branch, alone, which joins the points P_{i+1} with P_i, and l_i its length, that is, the distance (P_{i+1}, P_i). All the weights B'_i and B''_i are assumed to act in one vertical plane. Call B_i the resultant of all weights acting between and at $P_1, P_2, \cdots, P_i$ and M_i the resultant moment of all those weights with respect to P_i.

Instead of weights and moments we will use, for simplicity, the following quantities which have the dimensions of areas and volumes respectively:

$$\beta'_i = FB'_i, \qquad \beta''_i = FB''_i, \qquad \beta_i = FB_i, \qquad \mu_i = FM_i,$$

where [Opatowski, 1944a, equation (3)],

$$F = 4f'/(\pi \sigma_b) = 103 \times 10^{-5} f' G^{-5/4}. \tag{1}$$

We will maintain the name of forces for β's and of moments for μ's. The units are throughout the paper kg and cm. We have the following obvious relation:

$$\beta_{i+1} = \beta_i + \beta'_i + \beta''_{i+1}. \tag{2}$$

The weight acting at the free end of the primary branch is B''_1 and we must assume that it is $\neq 0$, otherwise we would run again into an infinite or imaginary deflection. This detail however may be easily taken care of by considering the very tip element of the primary branch as a secondary branch.

If r_i is the radius of the cross-section of the primary branch at P_i, the condition that the maximum bending stress in that cross-section be equal to σ_b/f' is (Timoshenko, 1940, pp. 209-210)

$$\mu_i = r^3_i, \tag{3}$$

whereas at a point P between P_i and P_{i+1}, at a distance x from P_i, that condition is (Blasius, 1914; Opatowski, 1945)

$$\mu_i + \beta_i x + \gamma \int_0^x (x - \xi)[r(\xi)]^2 \, d\xi = [r(x)]^3, \tag{4}$$

where $r(x)$ is the radius of the cross-section at x, and

$$\gamma = m'f'G/(250\,\sigma_b) = 323 \times 10^{-8}\, m'f'G^{-1/4}.$$

Equation (4) is an integral equation in $r(x)$, which differentiated twice with respect to x gives

$$3rr'' + 6r'^2 = \gamma r, \tag{5}$$

where the primes stand for derivatives with respect to x. The initial conditions are:

$$r(0) = r_i, \quad r'(0) = \beta_i/(3r_i^2). \tag{6}$$

The solution of equation (5) under the conditions (6) is the hyperelliptic integral

$$x = 3 \int_{r_i}^{r} [Z(r, r_i)]^{-1} r^2\, dr, \tag{7}$$

where

$$Z(r, r_i) = [1.2\,\gamma(r^5 - r_i^5) + \beta_i^2]^{1/2}.$$

The weight of the part of the primary branch between P_i and P_{i+1} is easily obtained from equation (7):

$$\beta'_i = Z(r_{i+1}, r_i) - \beta_i. \tag{8}$$

The equations (2), (3), (7), and (8) relate the radius of the cross-section of the primary branch to the weights B''_i of the secondary branches and to their mutual distances l_i. These equations provide a possibility of testing the principle of maximum strength on an actual branch and may be used also for calculating the safety factor f'. The applicability of the formulae is not limited to horizontal primary branches, because they may be used also for horizontal parts of curved branches. The theory could be easily extended to inclined or curved branches, but the purely statical considerations of mechanical strength are not sufficient to explain the curvature of a branch.

The function $r(x)$ is completely determined by the quantities B''_i, l_i and all the r_i's may be calculated successively from the equations (2), (3), (7), and (8). Such calculations involve however an evaluation of the hyperelliptic integral (7) which may be carried out through a power series expansion of $r(x)$. We obtain directly from equations (5) and (6):

$$r(x) = r_i + r'_i\, x + (r''_i/2)x^2 + (r'''_i/6)x^3 + \cdots \tag{9}$$

where

$$r'_i = \beta_i/(3r_i^2); \qquad r''_i = (\gamma/3) - (2r_i'^2/r_i);$$
$$r'''_i = (\gamma - 15r''_i)r'_i/(3r_i).$$

According to the theory, the secondary branches do not cause discontinuity in the radius of the cross-section, because the bending moment increases continuously from the free end towards the junction with the trunk (equation 3). One gets r_{i+1} from equation (9) putting $x = l_i$.

As a numerical example, let us consider a horizontal piece (p) of a primary branch between two consecutive secondary branches. Cut off the primary branch at a point P_i of (p) and let $r_i = 5$ cm be the radius of the cross-section at P_i. Let $B_i = 5$ kg be the weight of the part of the branch cut off (complete, that is, with secondary branches and leaves) and $M_i = 600$ kg cm the moment of B_i with respect to P_i. Let $m' = 2.5$, $G = 0.5$ so that $G^{1/4} = 0.84$. From equations (1) and (3) we get the safety factor

$$f' = 972\, G^{5/4}\, r_i^3/M_i = 85\,.$$

Therefore, $\gamma = 0.0008181$, $F = 0.2083$, $\beta_i = 1.042$. For $l_i = 25$ cm we get from equation (9)

$$r_{i+1} = 5 + 0.347 + 0.061 - 0.005 + \cdots = 5.4 \text{ cm}.$$

The convergence is good.

Since γ is small one could expand expression (7) in power series of γ, which would give

$$x = \beta_i^{-1}(r^3 - r_i^3) + \beta_i^{-3}(0.6 r_i^5\, r^3 - 0.225 r^8 - 0.375 r_i^8)\,\gamma + \cdots .$$

However, the convergence of this series is not better than that of expression (9) and the high powers of r make its use inconvenient.

The writer is indebted to Professor N. Rashevsky for his continuous interest in this work, to Professor A. S. Householder for the opportunity to discuss the main ideas of this paper at a seminar meeting of the University of Chicago, to Dr. H. D. Landahl, Mr. J. Nielsen, and Dr. W. S. McCulloch for valuable criticism and suggestions.

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MUSCULAR DYNAMICS AND MUSCULAR EFFICIENCY: I. THE ISOMETRIC LENGTH-TENSION DIAGRAM OF STRIATED SKELETAL MUSCLE

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The isometric length-tension diagram for individual fibers and for whole muscle is considered, and it is proposed that the tension p may be represented for any muscle whose fibers are parallel and not in series, in the form

$$p = f(x) + \beta\,\phi(\alpha, l, x),$$

where the form of ϕ is known and the same for all muscles, the parameters α and l are experimentally measurable, x represents the length, β the degree of activity of the muscle, and the form of $f(x)$ varies from muscle to muscle.

We wish to consider the muscle as the source of power for the operation of the bodily machinery. Consequently, our chief interest shall lie in the muscle as a whole, *in situ*. The importance of muscle lies not only in the fact that it alone drives the machinery in the performance of overt activity. On the contrary, even if we do not go so far as M. F. Washburn (1916) and identify all mental imagery with muscular movement, the work of E. Jacobson (1934) and others has made it abundantly clear that muscular activity of at least an incipient sort is intimately associated with even the "higher" thought processes, while at the same time certain fairly successful theories of discriminatory processes (Rashevsky, 1940; Householder, 1940; Householder and Landahl, 1944) have postulated for muscles a role very similar to that which M. F. Washburn attributes to it.

In nerve, considered with respect to its role in the reactions of the organism, the interest centers about the action-spike, its conduction and its transmission. Because of the all-or-none law and the phenomenon of refractoriness, nervous activity is quantized (McCulloch and Pitts, 1943), the principles of nervous coordination are expressible in terms of merely the occurrence or non-occurrence of each of a certain class of events (the firing of specified neurons) in each of a class of time-intervals (covering the life-time of the organism). It is true that the complexity of the structure of the nervous system and the shortness of the elementary time-intervals must necessitate the employment of statistical analyses (Landahl, McCulloch, and Pitts,

1943; Householder and Landahl, 1944), but the bases for a theory of nervous coordination seem to be conceptually simple.

But for the present, at least, there exists no such reduction of muscular activity to simple elements, and the great divergences of opinion among investigators, and their sharply discordant results, make it very difficult to discern a direction in which to look for a reduction.

We wish to consider the mechanical response of muscle, having in view principally the whole muscle *in situ*. The main object will be to arrive at quantitative formulations for describing, first, this response as a function of time and a functional of the stimulus, and second, the efficiency of the muscle, regarded as a machine for converting chemical energy into mechanical work, under the various conditions to which it may be subject. With this purpose in view we shall first examine, more or less in isolation one from the others, several sets of properties of the muscle, describing such formulations as have been proposed in the past, and attempting to revise or supplement these where possible.

The simplest set of properties is contained in the classical isometric length-tension diagram (cf., e.g., Fenn, 1925; Hill, 1926; Ramsey, 1944). In the diagram for resting muscle, the muscle is stretched by a given amount, and the resulting tension is plotted as ordinate against the length as abscissa. For the active muscle the muscle is first stretched, then subjected to tetanic stimulation without being permitted to shorten, and the maximal tension is then recorded. Upon stimulation the tension is ordinarily raised, but according to E. Weber ("Weber's paradox", 1846; reported, e.g., by W. O. Fenn, 1925) when the stretch is sufficiently great the tension may diminish.

Whether it is a single fiber or the whole muscle under consideration there must result a set of curves which depend upon at least one parameter for characterizing the stimulation (cf. Th. Christen, 1911). Let us consider one of them, supposing the temperature and other conditions to be held constant, and writing its equation

$$p = f(x). \tag{1}$$

There are other ways in which one could obtain a length-tension diagram. One could first stimulate and then stretch to length x, and one could vary the rate at which the stretch takes place, etc., and there is no reason *a priori* for supposing that one would always come out with the same tension p at any given length x, even though the muscle may at no time have been stretched enough to injure it. Thus E. Asmussen (1936) finds that if a fiber bundle is first stimulated and then stretched beyond about 25% of its normal length, without stimu-

lation and without tension, the tension becomes increasingly greater than that which is developed when the stimulation follows the stretch. This effect he associates with the fact that he finds the threshold of stretched muscle to increase with the amount of stretch, so that we may infer that in the prestretched bundle there are fewer fibers activated by the stimulus, and hence less tension developed. But it is not clear from E. Asmussen's results that, once a fiber is activated the subsequent dependence of its tension upon its length is in any way dependent upon the initial length or that hysteresis is otherwise evident to any substantial degree, nor is this evident from the work of previous investigators when the stretches are not extreme (Fenn, 1925). Moreover, while R. W. Ramsey and S. F. Street (1941) find that when a fiber is allowed to shorten too much (below about 2/3 its length at zero tension without stimulation) it then enters irreversibly a new condition (the "δ-state"), they deny the presence of hysteresis where the changes are not extreme. D. Brown (1936) reports, indeed, that the tension developed in isometric twitch increases with the initial tension, but it does not follow that this is the case in tetanic stimulation. It seems reasonable to suppose, therefore, that if we exclude extreme degrees of stretch and shortening (and perhaps extreme rates of stretch and shortening) the hysteresis will be negligible, and we may regard the unstimulated or the tetanically stimulated muscle or fiber as an elastic body for which the tension is a single-valued function of the length as given by equation (1).

If our supposition is legitimate, we may define the potential energy of the muscle at length x, when subject to the given mode of sustained stimulation, as

$$w(x) = \int_{x_0}^{x} f(\xi)\, d\xi ,$$

where x_0 is the lower limit of the range of reversibility. Alternatively, we may extend the range of definition of $f(x)$ for $x < x_0$ and define $f(x)$ on this range as the tension developed when the muscle is stimulated at the length of zero tension and then allowed to shorten to the length x. Then we may replace the above function by

$$w(x) = \int_{0}^{x} f(\xi)\, d\xi . \tag{2}$$

Clearly, then, if the muscle is allowed to shorten from a length x_1 to a length x_2 it is capable of doing work in amount $w(x_1) - w(x_2)$. If the muscle is allowed to shorten isotonically under tension $f(x_2)$ it will do mechanical work amounting to only $(x_1 - x_2) f(x_2)$, whence the difference must be dissipated as heat. Since $w' = f$, this differ-

ence is, by a standard theorem,

$$w(x_1) - w(x_2) - (x_1 - x_2)f(x_2) = \tfrac{1}{2}(x_1 - x_2)^2 f'(x), \qquad (3)$$

for some x satisfying $x_1 \geqq x \geqq x_2$. The amount of heat per unit of shortening is therefore $\frac{1}{2}(x_1 - x_2)f'(x)$, a quantity which vanishes with the amount of shortening. If the shortening takes place under some lesser, fixed, tension p and is suddenly arrested at the length x_2, then the heat liberated per unit of shortening is

$$f(x_2) - p + \tfrac{1}{2}(x_1 - x_2)f'(x_2).$$

This we may denote the viscous heat, though it is quite independent of the measure of the viscosity.

Now A. V. Hill (1938) finds that the amount of heat which is actually liberated by the stimulated muscle in the process of shortening—over and above the "maintenance heat" which is developed while no shortening occurs—is independent of the work which is performed, which is certainly not true of the viscous heat just defined. Granting this result, we must seek the explanation in the molecular mechanism of contraction (Brown, 1941), and in the ordinary thermodynamic effects (Hill and Hartree, 1920).

Determinations of the length-tension diagram have been undertaken by a number of investigators (see W. O. Fenn, 1925, for the earlier papers). Measurements by E. Weber (1846; reported by W. O. Fenn, 1925; Th. Christen, 1911; and others) indicated that

$$d^2p/dx^2 > 0: \qquad (4)$$

the increase in tension per unit of stretch increased with the amount of stretch ("Weber's law"). Th. Christen (1911) presents alternative theoretical functions for whole muscle, both satisfying (4), and both based upon formulas proposed by previous authors, but modified to eliminate certain formal difficulties. The first of these is taken from G. Weiss. Th. Christen's form is

$$dx/dp = a/[p + c], \quad p = c(e^{(x-s)/a} - 1). \qquad (5)$$

This is equivalent to

$$dp/dx = \beta\, e^{x/a}, \qquad (6)$$

according to which the ratio of the increment of tension to the increment of length is an exponential function of the length.

Th. Christen's other equation has the form

$$dp/dx = c + a(x - s), \quad p = c(x - s) + \tfrac{1}{2}a(x - s)^2, \qquad (7)$$

where the ratio of the increments is linear instead of exponential.

M. G. Banus and A. M. Zetlin (1938), on the basis of extensive measurements upon unexcited whole muscle (cat and frog gastrocnemius, frog sartorius, cat rectus), propose, in present notation,

$$\log p = kx + a ,$$

and find very close agreement. But this is essentially G. Weiss's equation which Th. Christen replaces by equation (5) in order to eliminate the absurdity at $p = 0$, and if we make a proper choice of the parameters, we may do likewise. Now M. G. Banus and A. M. Zetlin find that if the muscle-fibers are removed from the connective tissue sheath, a curve of almost identically the same form is obtained from this sheath alone. This may indicate either that virtually the whole tension of the resting muscle is due to the connective tissue sheath alone, or else that the length-tension diagram of the individual unstimulated muscle-fibers has the same form as that of the connective tissue sheath. While the somewhat earlier work of F. Sichel (1934) seemed to indicate that the diagram for the individual unstimulated fibers is linear, E. Asmussen (1936) and R. W. Ramsey and S. F. Street (1940) criticize his methods and obtain, for individual fibers and for small bundles, curves which closely resemble those of M. G. Banus and A. M. Zetlin. According to R. W. Ramsey and S. F. Street, while some of the curves they obtained were exponential they were not all so, although they did all exhibit the upward concavity in accordance with Weber's law.

R. W. Ramsey and S. F. Street (1941) attribute all the tension exerted by the unstimulated stretched fiber to the sarcolemma, since they have succeeded in severing the myo-fibrils by local pressure, thus obtaining a segment of clear sarcoplasm, and found the length-tension diagram of the injured fiber to be almost identical with that obtained for it prior to the injury. A further detail which strongly supports this supposition is the fact that parasites have been observed freely moving within the fiber (Cowdry, 1938). Both observations seem to throw doubt on the measurements of F. Buchthal and J. Lindhard (1938-39) indicating that during passive stretch the isotropic and the anisotropic segments are stretched in different proportions, unless we are to suppose that the sarcolemma has itself a segmental character.

A. Bairati (1937) finds by histological examination that the sarcolemma consists of virtually inextensible anastomosing fibrils imbedded in a matrix, these fibrils running, some parallel to the axis of the fiber, some obliquely. His conception seems to be that the fibrils which run obliquely form a kind of network with meshes which we may picture schematically as rhombic, that the longitudinal fibrils are

attached to opposite vertices of these rhombi, some being connected to one, some to the other tendinous termination of the fiber, and that the tension in stretch is due to the distortion of this net. Before stretch these fibrils are described as wavy. A. Bairati and also R. W. Ramsey and S. F. Street (1940) suggest that the form of the length-tension diagram of the resting fiber may be explainable on the basis of the gradual taking up of the slack and subsequent stretch of these fibrils. However, some of these fibrils must be taut even at the resting length since otherwise we could not understand the return to this length (on this basis) when the external tension is released. We cannot introduce sliding friction, as A. Bairati seems to do, to explain the tension in stretch for an analogous reason—some elastic tension is required to return the fiber to its resting length. Now if we suppose that the longitudinal fibers are inextensible and only the oblique fibers are extended, since the length of an oblique fibril is of the order of the radius of the fiber, this being only about one-tenth the length of the fiber and of the order of one-tenth of the amount of stretch the fiber can sustain reversibly, the extent to which these oblique fibrils would be stretched would be quite enormous. It seems much more likely that the fibrils act as a safety catch designed to prevent altogether a stretch exceeding the elastic limits of some other elastic mechanism which is normally operating.

This leaves us, by successive elimination, with the matrix in which the sarcolemmal fibrils are imbedded as the only possible elastic mechanism in the resting muscle-fiber. Apparently but little is known of this, and there seems to be little profit in presenting anything but a phenomenological equation such as Th. Christen's for describing its elastic behavior. But there is certainly no occasion for surprise in the failure of Hooke's law over the wide ranges of stretch employed, and an explanation of its failure is neither more nor less essential then would be an explanation of its validity if it had been found to hold. It is, however, interesting to note the resemblance of the length-tension diagram to that of rubber (James and Guth, 1944), especially in view of the well-known fact that both muscle and rubber contract on heating (Hill and Hartree, 1920).

When the muscle-fiber is stimulated the length-tension diagram differs quite considerably, passing through a maximum and a minimum and later following the resting diagram quite closely. While E. Asmussen (1934, 1936) and others think that the all-or-none law is a property of the motor end-plate but not of the fiber, the greater number of investigators seem to be of the contrary opinion (Gelfan and Gerard, 1930; Ramsey and Street, 1940), and we shall adopt the latter hypothesis. Hence associated with any fiber are but two dia-

grams, that corresponding to the state of rest and that corresponding to the state of complete activity, at least if the frequency of stimulation is high enough to prevent relaxation between stimuli. According to R. W. Ramsey and S. F. Street (1940, 1941) when the ordinates of the diagram for rest are subtracted from those for activity, and the ordinates and abscissas taken to represent fractions of maximal tension and of rest length, respectively, the resulting differences agree very closely from fiber to fiber, all possessing a maximum at (1 , 1) and intercepting the horizontal axis at 2. According to R. W. Ramsey (1944) the failure of this curve to pass through the origin is due chiefly to the resistance of the sarcolemma.

Presumably, therefore, the isometric length-tension diagram of the whole muscle should involve a single parameter only, which can be taken as the proportion of fibers simultaneously activated, contrary to Th. Christen's (1911) assumption that two are required. It is hard to see how two independent parameters could be involved unless we suppose the distinct fibers to have sensibly different curves and to be provided with a neural mechanism capable of stimulating the fibers independently. Th. Christen argues that one can voluntarily exert a predetermined (limited) amount of tension irrespective of position and one can also assume a predetermined position (with muscles at fixed lengths) irrespective of tension. But for this to be possible one need only suppose that two types of kinaesthetic receptors are available, one for tension and one for position, both suitably linked with the motor neurons—the single parameter may itself be a function of two others—and there is evidence for such distinct receptors (Matthews, 1933).

If the contractile mechanism is linked in parallel with the static elements which operate alone when the muscle is at rest, if the muscle consists of parallel fibers (none in series) of approximately equal lengths, and if the tendinous connections are of very high elasticity, let us write for the whole muscle at rest

$$p = f(x) , \tag{8}$$

where f is perhaps exponential in form. Suppose that each fiber is only α times as long as the whole muscle, the rest consisting of tendinous connections, and let

$$\pi = \phi(\xi) \tag{9}$$

represent the tension taken up by the contractile elements of an individual active fiber, where π represents a fraction of the maximum for the fiber and ξ represents the multiple of the resting length. If l is the resting length of the whole muscle, then $\alpha\, l$ is the resting length

of the fiber and therefore the length x of the whole muscle is given by

$$x = \alpha \xi l + (1 - \alpha) l ,$$

or

$$\xi = [x - (1 - \alpha) l] / (\alpha l) . \tag{10}$$

Hence

$$\pi = \phi\{[x - (1 - \alpha) l] / (\alpha l)\} . \tag{11}$$

Therefore, if β represents the intensity of activation, being equal to the number of fibers activated multiplied by the maximal tension contributed by the contractile elements of each, the isometric length-tension diagram of the whole muscle should have the form

$$p = f(x) + \beta \phi\{[x - (1 - \alpha) l] / (\alpha l)\} . \tag{12}$$

The parameters l and α are directly measurable; according to R. W. Ramsey (1944) the function ϕ is very nearly the same for all fibers. There remains only the single parameter β and the additive function $f(x)$ which is independently determinable and appears to be approximately exponential in many cases. Note that we here employ no assumption whatever as to the source (whether sarcolemma or sarcoplasm) of the elastic properties of the resting muscle described by the function $f(x)$.

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SOME NUTRITIONAL AND EXCRETIONAL INTERACTIONS AND THE GROWTH OF AN ORGAN OR COLONY

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Following the general form for the differential equation of organism and colonial growth, there is derived a rational formulation for the growth of a bounded cell community (e.g., an organ) equipped with a food supply and a waste removal mechanism. It is shown how, from the integral form and an empirical curve, the vital coefficients of the equation can be derived. Changes to be expected in these coefficients are discussed, and the analytic methods for assessing them are set forth. It is hoped that these equations and similar ones will make it possible to relate empirical curves to the mathematico-biophysical theory of the cell.

In the following analysis we will examine the growth of a cell community, spatially bounded and equipped with a mechanism which supplies its food and removes its wastes. In the course of our derivations it will be necessary to make many gross assumptions and approximations. We feel that no apology is necessary for this policy provided that the temporary nature of the work is fully realized. Our main thesis will be in line with the notion set forth in a previous paper (Morales and Shock, 1942): A cell has its own fundamental growth rate. In the proximity of other cells it suffers interactions which change this rate. The reduction of food supply per cell, irrespective of the mechanism, and the increased concentration of waste products, irrespective of the mechanism, always give rise to *reductions* in the growth rate of the community. If one identifies "food" with "reactant", and "waste" with "product", then the problem is reduced to one of the chemical kinetics in which diffusion is recognized as a factor. In this sense our analysis is a gross version of the fundamental theory of cell division developed in Mathematical Biophysics (Rashevsky, 1938; 1940); in fact we hope that analyses of the type to be presented will provisionally link experimental work with the mechanical theory of the cell, and thus open to the latter a

* The opinions or assertions contained herein are the private ones of the writers, and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

vast array of guiding data in the form of growth curves of communities.

For the sake of concreteness we will use the terminology proper to a well defined homogeneous cell community, such as a vertebrate organ, equipped with an arterial and venous food supply. It will be clear as we proceed, however, that this interpretation of the situation is not unique. Furthermore, we will carry out the derivations considering only the interactions of food supply; later we shall readily show that the same remarks apply *mutatis mutandis* to the interactions of waste accumulation.

Let N be the number of cells in the organ at time, t. Then the rate of proliferation *per cell* is dN/Ndt. Under the assumption that there is a fundamental proliferation rate which is subject to the influences, for example, of hormones or radiations on the mitotic mechanism, but not to other causes, we have provisionally that

$$\frac{1}{N}\frac{dN}{dt} = \text{Constant} + \cdots \equiv a + \cdots. \tag{1}$$

Suppose, furthermore, that the cells ingest from their medium an amount of food which is appreciable in comparison with the amount supplied to each cell by the blood*. If

R li. sec.$^{-1}$ = rate of blood flow into the organ, and
$x^{(i)}$ moles li.$^{-1}$ = concentration of the i-th nutrient in the arterial blood,

then

$Rx^{(i)}$ moles sec.$^{-1}$ = $T^{(i)}$ = total influx of food, and
$T^{(i)}/N$ moles sec.$^{-1}$cell^{-1} = food available per cell.

Let us imagine that each cell actually ingests $B^{(i)}$ moles sec.$^{-1}$cell^{-1} of the i-th nutrient. Then the total amount of food made unavailable by this mechanism on the average is $B^{(i)}N$ moles sec.$^{-1}$. The resulting drop in the steady state concentration of the nutrient must be proportional to $B^{(i)}N$, and therefore the negative effect on the rate of proliferation per cell is likewise proportional to it. Since the numerical value of B is not to be discussed, we omit the introduction of a proportionality constant, and write merely

$$(\text{Effect})^{(i)} = -B^{(i)}N \ .$$

Next we shall study blockage of nutrient streams by regarding it as an *immobilization* effect which all cells exert on their neighbors

* In the author's opinion this could be ascertained experimentally from thermal studies such as have been made for certain amphibian organs (Morales, 1942).

even though they do not actually ingest such food in competition. Thus we may consider any nutrient molecule to be in the force field of many cells. Consider any two such competitors. The net force with which either attracts the molecule is less than it would be were the other competitor not present. The net effect is a diminished food supply per second for either of the two cells. The same result would obtain if, through the influence of the neighbor, the concentration near one cell had been lowered by a fictitious amount. Treating the problem this way circumvents the more exact but almost hopeless vectorial analysis of the situation.

Choosing spherical coordinates, r, θ, ϕ, with origin at the n-th cell, we proceed by letting $K_n^{(i)}(r)$ moles sec.$^{-1}$ cell^{-2} be the immobilization effect of the n-th cell on any cell. Let $\rho(r, \theta, \phi)$ be the cell density in cells cm^{-3}. Then the effect of the n-th cell on *all* cells of the organ will be

$$\int_{\text{organ}} K_n^{(i)} \rho_n \, dv \qquad \text{moles sec.}^{-1} \text{ cell}^{-1},$$

and the total interaction effect would be

$$E = \sum_{n=1}^{n=N} \int_{\text{organ}} K_n^{(i)} \rho_n \, dv \, . \tag{2}$$

However, it is clear that to evaluate each integral the origin would have to be shifted from cell to cell for all N cells, and in each case the equation of the surface which gives the organ shape (hence the limits of integration) will be different. We avoid this difficulty in the following approximate way: Suppose that for the n-th cell the equation of the organ surface is available in the form

$$R_n = r_n(\theta, \phi).$$

We then define the mean radius of the surface "viewed" from the n-th cell as

$$\bar{r}_n = \frac{1}{4\pi} \int_0^{2\pi} \int_0^{\pi} r_n \, d\theta \, d\phi \, ,$$

and the mean of these means as

$$r_0 = \frac{1}{N} \sum_{n=1}^{n=N} \bar{r}_n .$$

Thus as far as the n-th cell is concerned, we regard the organ as a sphere of radius r_0 with center on the n-th cell, and the integral (2) can be written as

$$E = \sum_{n=1}^{n=N} \int_0^{r_0} \int_0^{\pi} \int_0^{2\pi} K_n^{(i)}(r)\ \rho_n(r, \theta, \phi)\, r^2 \sin\theta\, dr d\theta\, d\phi . \qquad (3)$$

We will regard equation (3) as the general form for the nutrient immobilization effect. In the event that ρ be a constant, say $\bar{\rho}$, independent of coordinates, equation (3) reduces to

$$E = 4\pi \bar{\rho} \sum_{n=1}^{n=N} \int_0^{r_0} K_n^{(i)}(r)\ r^2\, dr . \qquad (4)$$

This is certainly a justifiable assumption for many organs. In this case, if V is the volume of the organ, the gross density is merely

$$\bar{\rho} = N/V.$$

Although many organs are quite uniform histologically, it is well known that at any one time there are important differences in amount of metabolic activity from region to region within them, consequently $K_n^{(i)}(r)$ will generally be different for each cell. If we assume a mean value for this quantity, or if for some reason we believe the organ in question to be physiologically homogeneous,* then equation (4) may be simplified further to

$$E = N^2 \left(\frac{4\pi}{V} \int_0^{r_0} K^{(i)}(r)\ r^2\, dr \right) . \qquad (5)$$

The factor in parentheses includes a definite integral not containing the dimension "cell", consequently it follows that *no matter what is the quantitative law of interaction,* $K^{(i)}$, *the total interactive effect,* E, *is proportional to the square of the number of cells,* and the interactive coefficient or "vital coefficient" (Kostitzin, 1939) is a function of the organ or colony size, not necessarily of cell number. The integral of equation (5) can be evaluated for some simple laws of action, and it is interesting to consider two of these because they may have some bearing on the more fundamental theory referred to initially. If

* This is very likely true of glandular tissues. To some extent a similar qualification is necessary in considering "*B*", but for that case the mean value of *B* is easy to compute from arteriovenous differences.

$$K^{(i)}(r) = a^{(i)} r^{-m} \quad (m > 0),$$

$$E^{(i)} = N^2 \left[\frac{4\pi a^{(i)}}{3-m} \right] \frac{r_0^{(3-m)}}{V}, \tag{6}$$

in which it can be easily shown that $m < 3$ must hold. If, on the other hand,

$$K^{(i)}(r) = a^{(i)} e^{-\lambda^{(i)} r}$$

with

$$\lambda^{(i)} > 0,$$

then

$$E^{(i)} = N^2 (4\pi a^{(i)}) \frac{\frac{2}{\lambda^{(i)3}} - \left\{ \frac{r_0^2}{\lambda^{(i)}} + \frac{2r_0}{\lambda^{(i)2}} + \frac{2}{\lambda^{(i)3}} \right\} e^{-\lambda^{(i)} r_0}}{V}. \tag{7}$$

In both equations (6) and (7) it is probable that E will increase with time unless the organ is characterized by anomalously large cells and a low proliferation rate.* The vital coefficient of N^2 which we may henceforth call $C^{(i)}$ such that $E^{(i)} = -C^{(i)} N^2$, will tend to diminish in both equations (6) and (7), if we regard V as of the order of r^3_0.

In any event, we now have reasonable grounds for setting the sum total of this effect as equal to

$$-C^{(i)} N^2 \text{ moles sec.}^{-1} \text{ cell}^{-1}.$$

Returning now to our original problem, we see that the i-th food *not* unavailable per cell per second is

$$\frac{T^{(i)}}{N} - B^{(i)} N - C^{(i)} N^2 \text{ moles sec.}^{-1} \text{ cell}^{-1}$$

and for f foods $(i = 1, 2, \cdots f)$ it is

$$\sum_{i=1}^{i=f} \frac{T^{(i)}}{N} - B^{(i)} N - C^{(i)} N^2.$$

Let us now see to what extent these remarks are applicable to the elimination of wastes. Since blood is incompressible, the rate at which blood flows out is R li. sec.$^{-1}$ (actually this should be blood *plus lymph*, but for purposes of formulation this is immaterial). If $x^{(j)}$ is the concentration of the j-th waste in the venous blood, then $T^{(j)} = Rx^{(j)}$ moles sec.$^{-1}$ is the total efflux of waste j, and $T^{(j)}/N$ moles sec.$^{-1}$ cell^{-1}

* This follows because N is of the order of r^3_0.

is the waste removed per second per cell. Suppose each cell produces per second an amount of waste equal to $B^{(j)}$. The total of such effects is $B^{(j)}N$. For converse reasons to those outlined above, the immobilization of wastes gives an effect proportional to $C^{(j)}N^2$. Now the total amount of waste accumulating or affecting the steady state waste concentration should be proportional to

$$-\sum_{j=1}^{j=w} = \frac{T^{(j)}}{N} + B^{(j)}N + C^{(j)}N^2 \text{ for } w \text{ wastes}, 1, \cdots w.$$

The rate prescribed by the tentative equation (1) is now modified by the positive effect of excess food, and the negative effect of excess waste to give

$$\frac{1}{N}\frac{dN}{dt} = a + \sum_{i=1}^{i=f}\left(\frac{T^{(i)}}{N} - B^{(j)}N - C^{(j)}N^2\right) - \sum_{j=1}^{j=w}\left(-\frac{T^{(j)}}{N} + B^{(j)}N + C^{(j)}N^2\right), \tag{8}$$

or, rearranging and using the fact that $T = Rx$,

$$\frac{dN}{dt} = \left\{\left(a + R\frac{\sum_i x_i + \sum_j x_j}{N}\right) - \left(\sum_i B^{(i)} + \sum_j B^{(j)}\right)N - \left(\sum_i C^{(i)} + \sum_j C^{(j)}\right)N^2\right\}. \tag{9}$$

To our degree of approximation we are not justified in attempting to distinguish between the effects of various metabolites, as would be suggested by the form (9). Accordingly we substitute each of the expressions in parentheses of form (9) by gross coefficients, A, B, and C, remembering, however, the general nature of these quantities. This leads finally to the differential equation of the growth of the organ:

$$\frac{dN}{dt} = N(A - BN - CN^2). \tag{10}$$

Before such an expression can be of any but speculative value, methods must be developed to test it experimentally. In the case of equation (10) this can fortunately be done in complete fashion. As we shall discuss below, variations in A, B, and C are to be expected in

the course of the life-span, but in an approximate general way (or under certain experimental conditions, in a *rigid* way) the general integral of equation (10) will not differ seriously from the integral of (10) in the special case of A, B, and C are constants. As a first step, then, we will study equation (10) under the assumption of constant vital coefficients.

The slope at the origin is evidently zero, as it should be for analytic reasons (Winsor, 1934). It is again zero when

$$N = \frac{-B \pm \sqrt{B^2 + 4AC}}{2C}.$$

Of these only the positive root has physical meaning. We denote this positive root by N_∞. Differentiating equation (10) once more,

$$\frac{d^2N}{dt^2} = \frac{dN}{dt}(3CN^2 + 2BN - A).$$

Evidently $d^2N/dt^2 = 0$ when $dN/dt = 0$, i.e., at the origin and for $N = N_\infty$. It is also zero when

$$N = \frac{-B \pm \sqrt{B^2 + 3AC}}{3C}.$$

We denote the only physically significant root by N_I. Thus it appears that similar to the simpler so-called "logistic" function, this equation gives one asymptote and one inflection between zero and infinity which need not be so that $2N_I = N_\infty$.

The expressions for N_∞ and N_I make it possible to write B and C in terms of these quantities and of A. Thus

$$\begin{aligned} C &= \frac{1}{N_I N_\infty} \frac{2N_I - N_\infty}{2N_\infty - 3N_I} A \\ B &= \frac{1}{N_I N_\infty} \frac{N_\infty^2 - 3N_I^2}{2N_\infty - 3N_I} A. \end{aligned} \tag{11}$$

Let us now consider the direct integration of expression (10). This yields by elementary methods

$$\tfrac{1}{2} \log \frac{N^2}{A - BN - CN^2} + \frac{B}{\sqrt{-q}} \tanh^{-1} \frac{2CN - B}{\sqrt{-q}} = At + G', \tag{12}$$

where G' is a constant of integration and $-q = B^2 + 4AC$. Making

use of the expressions derived above for N_{00} and N_I, we readily transform expression (12) to give

$$\tfrac{1}{2}\log\frac{N^2}{N_\infty N_I(2N_\infty - 3N_I) - (N_\infty{}^2 - 3N_I{}^2)N - (2N_I - N_\infty)N^2} + \cdots$$
$$+\frac{N_\infty{}^2 - 3N_I{}^2}{(N_\infty - 3N_I)(N_\infty - N_I)}\tanh^{-1} \qquad (13)$$
$$\times\frac{2(2N_I - N_\infty)N + (N_\infty{}^2 - 3N_I{}^2)}{(3N_I - N_\infty)(N_\infty - N_I)} = At + G.$$

It follows that the constant A and the intercept G are obtainable from a plot of the appropriate function of N_I, N_∞, and N vs. time; consequently, in view of expression (11), all vital coefficients are determinate from experimental data. This concludes our derivation for the special case.

When, in accordance with expectation, A, B, and C are varying in time, their changes can be followed by analyzing the empirical curve. A method of doing this for the general growth equation is discussed elsewhere (Morales, 1944, in press); so it will suffice here to present the application to the particular problem at hand. If the differential operator, H, is defined as

$$H^0 = 1$$
$$H^1 = \frac{1}{\dfrac{dN}{dt}}\frac{d}{dt},$$

then, for instance, *at* (N, t):

$$B = -\frac{\begin{vmatrix} N & H^0\dfrac{dN}{dt} & N^3 \\ 1 & H^1\dfrac{dN}{dt} & 3N^2 \\ 0 & H^2\dfrac{dN}{dt} & 6N \end{vmatrix}}{\begin{vmatrix} N & N^2 & N^3 \\ 1 & 2N & 3N^2 \\ 0 & 2 & 6N \end{vmatrix}}$$

and analogously for A and C. Thus it is clear that from the em-

pirical data it is always possible to obtain the vital coefficients.

Let us now return to a consideration of the physiological basis of our equation:

$$\frac{dN}{dt} = N\left\{\left(a - \frac{Rx}{N}\right) - BN - CN^2\right\}.$$

If our hypotheses hold exactly, then of course relation (12) will hold exactly. However, this is not to be expected, nor in fact is it particularly desirable in the sense that a *perfect* fit would not substantiate our analysis as well as a fit which deviated in a certain way. The reason for this lies in the fact that we have not presumed the vital coefficients to be *strictly* constants. We consider these in turn:

The coefficient (C). As already stated, we rather expect that this coefficient shall diminsh during life in the case of a "typical" vertebrate organ such as the liver or pancreas. The factor K of C should furthermore be labile with respect to radical changes in type of metabolism or to very serious geometrical rearrangements as in early foetal life.

The coefficient (B). This is the vital coefficient related directly to the gross metabolism of the cell, and consequently its mode of variance will depend on the type of organ. The following general remark, however, would seem to hold true for all organs: There should be a sudden rise in B coincident with the initiation of actual function, and again the initiation of the thyroxine effect should be reflected in an increased B. For the rest of life B should be virtually a constant. It is quite conceivable that the rapid rise in B should be the best index of the inception of function.

The quantity (a). Two tangible remarks may be about a, and it may well be that they express the operation of the same phenomenon. As yet unpublished data suggests that, in the liver, growth hormone causes a specific rise in a, and lactogenic hormone likewise but to a lesser degree. The mechanical theory of the cell developed by Professor Rashevsky and his associates predicts that in the fundamental respiratory metabolism of the cell any shift favoring anaerobic glycolysis should increase dN/dt. This effect should be specifically observable in a.

The quantity (Rx/N). This is a coefficient of considerable interest, for it embodies the effect of the circulatory system and forms the basis for a type of experimental analysis which is discussed elsewhere (Kreutzer and Morales, in preparation). The circulatory supply might be said to be "in gear" when it grows in proportion to the number of cells which it feeds and whose wastes it removes. Mathematically this amounts to setting $R = kN$. In this case Rx/N is a true

constant as long as the composition of the blood does not change in nature (x, constant). There are certain important cases in which the circulation runs "out of gear" with the organ. One of these occurs in the early stages of development, when the organ cells proliferate ahead of blood vessels; a second such circumstance arises following the extirpation of part of the organ, leaving the blood supply intact; finally, in one classic case at least (Higgins, Mann, and Priestly, 1932) it was possible experimentally to enrich the blood supply to an organ and observe the result on growth. In all of these cases $R \rightarrow kN$ with time. With the exception of purely temporary disengagements like these we believe that $R = kN$, and T/N is a true constant.

In closing we should like to reiterate that studies of this sort, with the aid of experimental data, may aid in elucidating the general nature of population growth. They also are illustrative of methods that offer the possibility of drawing inferences regarding individual unit behavior from observing the more accessible behavior of the population. In the latter capacity, we hope they may serve the solution of the "major problem", namely, to understand the mechanism of the single cell.

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A PROBLEM IN THE MATHEMATICAL BIOPHYSICS OF BLOOD CIRCULATION: I

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The standard approximation method used in mathematical biophysics is applied to the problem of flow of an incompressible viscous fluid in an elastic distensible tube. It is found that the wall of the tube may perform damped transversal harmonic oscillations due to that flow. The phenomenon is independent of the viscosity, the latter contributing only a damping factor. While, due to rather rough approximations, the practical applicability of the equation derived is rather limited, it is suggested that they may give a clue to the understanding of vibrations of the walls of blood vessels which long ago have been suggested as the possible source of some hemic murmurs.

The hydrodynamics of viscous flow still presents a large number of difficult theoretical problems, even in relatively simple cases. The hydrodynamics of blood flow offers additional difficulties because of the non-rigidity of the blood vessels. In any ordinary hydrodynamical problem, even for ideal fluids, the shape and size of the tube through which the fluid flows enters into the boundary conditions of the system of partial differential equations which describe the flow. In case of a distensible tube like a blood vessel, the size and shape of the boundary are themselves determined by the distribution of velocities and pressures which in their turn are determined by the boundary conditions. Problems of that nature, not unfamiliar to the mathematical biophysicist, lead to complicated, usually non-linear, integro-differential equations or more general equations in functional derivatives. Exact solutions of such equations may well be considered as hopeless at the present time. It is therefore indicated to use some crude approximation method similar to the standard one in mathematical biophysics. The results thus obtained represent only very rough relations between average quantities, but they give at least some insight into the phenomena studied.

The most important contributions to the hydrodynamics of blood flow have been made in the classical investigations of O. Frank (1899; 1905; 1920; 1926). Frank's main interest centers on the problem of propagation of pressure waves. The problem of vibrations of the elastic walls of the blood vessels is also to some extent treated by Frank. Frank goes back to the differential equations of viscous flow,

and simplifies them by making some plausible idealized assumptions.

In this paper we shall attempt to apply to this field the approximation method which has been so successfully used in other problems of mathematical biophysics. The problem of vibrations of the blood vessels can, as we shall see, be treated rather simply by this method, leading to expressions for the frequency which is simpler than the one obtained by Frank. In subsequent papers we shall treat by a similar method different aspects of the problem. The results of this paper indicate the possibility of vibrations with frequencies within the audible range and thus suggest a possible explanation of some hemic murmurs.

As a preliminary problem we must discuss the relation between the radius of the blood vessel and the pressure which its elastic wall exerts on a liquid contained inside.

For simplicity, consider the blood vessel as an elastic tube stretched radially along a sufficient length so that its form remains essentially cylindrical.

Let R_0 be the radius of a blood vessel when it is not stretched at all. The actual radius R is usually several times larger. Consider a piece of blood vessel of length 1. If under the action of an internal pressure p the radius increases by the amount dR, the work done by p is equal to $2\pi pRdR$. If δ is the thickness of the wall, then the axial cross-section is equal to δ, and let $\delta << R_0$. The relative elongation of the circumference when the vessel is stretched from R_0 to R is $\frac{R-R_0}{R_0}$. Hence, if E is the elastic modulus of the wall and if we assume Hooke's law to hold for rather large relative elongations, we have for the elastic force

$$F = E\,\delta\,\frac{R-R_0}{R_0}. \tag{1}$$

When the radius increases from R to $R + dR$, the circumference increases by $2\pi dR$, and the work done by the force F is equal to

$$2\pi E\,\delta\,\frac{R-R_0}{R_0}\,dR. \tag{2}$$

Let p_e be the elastic pressure due to the force F. When the radius increases by dR, the work done by p_e is equal to $-2\pi p_e RdR$. This must be equal to expression (2). Hence

$$p_e = -p = -E\,\delta\left(\frac{1}{R_0}-\frac{1}{R}\right). \tag{3}$$

For $R = R_0$, when the tube is unstretched, $p = 0$. When $R = \infty$,

$$p_e = p_c = \frac{E\,\delta}{R_0}. \tag{4}$$

In other words, assuming Hooke's law to hold over any range of stretching, equation (4) gives the critical pressure at which the vessel would burst. Actually, due to deviations from Hooke's law, the vessel may break at much lower pressures.

For $p < p_c$ the equilibrium radius R^* of the tube is determined from equation (3), in which p is considered as given.

If a viscous fluid flows through the tube in a stationary state, the pressure p drops in the direction of flow. Therefore, the radius R^* will vary along the axis. The law of this variation will be discussed in a subsequent paper. Too rapid a variation of R^* in the axial direction will result in additional elastic forces due to longitudinal stretching of the wall, and the expression for p_e will be different from that given by equation (3). We shall confine ourselves here only to cases when R^* varies so little along the axis that at each point equation (3) can be applied. Denoting by p_{01} and p_{02} the hydrodynamical pressures in the stationary state at two points, 1 and 2, and by R_1^* and R_2^* the corresponding radii, we have

$$p_{01} - E\,\delta\left(\frac{1}{R_0} - \frac{1}{R_1^*}\right) = 0; \quad p_{02} - E\,\delta\left(\frac{1}{R_0} - \frac{1}{R_2^*}\right) = 0. \tag{5}$$

A periodical deformation along the tube may be represented very roughly for very small amplitudes by a set of straight line segments,

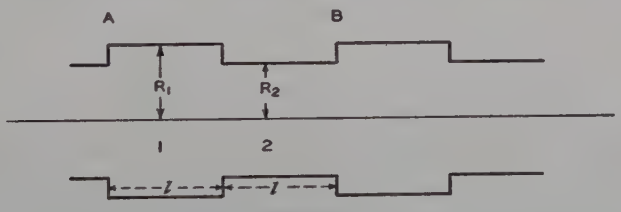

FIGURE 1

as shown in Figure 1. The quantity $2l$ may be considered as the wave length. Defining R_1 and R_2 as indicated in Figure 1, put

$$\Delta_1 = R_1 - R_1^*; \quad \Delta_2 = R_2 - R_2^*, \tag{6}$$

and let Δ_1 and Δ_2 be very small. Then we may neglect possible additional elastic forces due to the radially directed parts of the tube wall, and still apply equations (3) and (5). For each half wave length of the tube we may now write the equations of motion. Denote by ρ_1 the

density of the wall, and by p_1 and p_2 the actual pressures which will differ very slightly from the stationary state values p_{01} and p_{02}, so that

$$p_1 = p_{01} + (\Delta p)_1; \quad p_2 = p_{02} + (\Delta p)_2, \tag{7}$$

the quantities $(\Delta p)_1$ and $(\Delta p)_2$ being very small. The equations of motion now are:

$$\begin{aligned} 2\pi R_1 \delta \rho_1 l \frac{d^2 R_1}{dt^2} &= 2\pi l R_1 \left[p_1 - E\delta \left(\frac{1}{R_0} - \frac{1}{R_1} \right) \right]; \\ 2\pi R_2 \delta \rho_1 l \frac{d^2 R_2}{dt^2} &= 2\pi l R_2 \left[p_2 - E\delta \left(\frac{1}{R_0} - \frac{1}{R_2} \right) \right]; \end{aligned} \tag{8}$$

or

$$\begin{aligned} \delta \rho_1 \frac{d^2 R_1}{dt^2} &= p_1 - E\delta \left(\frac{1}{R_0} - \frac{1}{R_1} \right); \\ \delta \rho_1 \frac{d^2 R_2}{dt^2} &= p_2 - E\delta \left(\frac{1}{R_0} - \frac{1}{R_2} \right). \end{aligned} \tag{9}$$

Introducing equations (6) and (7) into equations (9), expanding the right hand sides, preserving only terms linear in Δ_1 and Δ_2, and remembering equations (5), we find

$$\begin{aligned} \delta \rho_1 \frac{d^2 \Delta_1}{dt^2} &= -\frac{E\delta}{R_1^{*2}} \Delta_1 + (\Delta p)_1; \\ \delta \rho_1 \frac{d^2 \Delta_2}{dt^2} &= -\frac{E\delta}{R_2^{*2}} \Delta_2 + (\Delta p)_2. \end{aligned} \tag{10}$$

Unless the wave length $2l$ is very large, R_1^* and R_2^* will be practically equal. If we consider under those conditions such a deformation of the tube which preserves the constancy of the volume, then

$$\Delta_1 = -\Delta_2. \tag{11}$$

Introducing this into equations (10), subtracting the second equation (10) from the first and putting $(1/R_1^{*2} + 1/R_2^{*2}) = 2/\overline{R}^{*2}$, where $\overline{R}^*$ is an average value for the whole wave length, we find:

$$2\delta \rho_1 \frac{d^2 \Delta_1}{dt^2} = -\frac{2E\delta}{\overline{R}^{*2}} \Delta_1 + (\Delta p)_1 - (\Delta p)_2. \tag{12}$$

As the tube in region 1 contracts at the rate $d\Delta_1/dt$, the total volume of the region varies at a rate $2\pi \bar{R}^* l\, d\Delta_1/dt$. This expels a total amount of liquid, of density ρ, $2\pi\rho \bar{R}^* l\, d\Delta_1/dt$ from region 1. If the total flow through the tube is maintained constant so that at the left end (Figure 1) the velocity is constant, this increases the velocity at the right end of region 1 by $-(2l/\bar{R}^*)(d\Delta_1/dt)$. Hence denoting by v_1 the *average* velocity in region 1, and by v the average constant stationary velocity, we have

$$v_1 = v - \frac{l}{\bar{R}^*}\frac{d\Delta_1}{dt}. \tag{13}$$

Similarly, we have for region 2

$$v_2 = v - \frac{2l}{\bar{R}^*}\frac{d\Delta_1}{dt} - \frac{l}{\bar{R}^*}\frac{d\Delta_2}{dt} = v - \frac{l}{\bar{R}^*}\frac{d\Delta_1}{dt} = v_1. \tag{14}$$

Hence

$$\frac{dv_1}{dt} = -\frac{l}{\bar{R}^*}\frac{d^2\Delta_1}{dt^2}; \quad \frac{dv_2}{dt} = -\frac{l}{\bar{R}^*}\frac{d^2\Delta_1}{dt^2}; \tag{15}$$

and therefore, for the derivative of the average velocity $\bar{v} = (v_1 + v_2)/2$ over the whole wave length we have

$$\frac{d\bar{v}}{dt} = -\frac{l}{\bar{R}^*}\frac{d^2\Delta_1}{dt^2}. \tag{16}$$

We shall now use an approximate form of the Stockes-Navier equations for the motion of liquid contained in the region AB (Figure 1).

The total acceleration of a fluid particle is the sum of the "substantial" acceleration $\partial v/\partial t$ and of the "convective" acceleration

$$v \operatorname{grad} v = \tfrac{1}{2} \operatorname{grad} v^2. \tag{17}$$

The average substantial acceleration of the liquid may be put equal to $d\bar{v}/dt$. The average value of the convection acceleration is

$$\tfrac{1}{2}\frac{v_2^2 - v_1^2}{l} = \frac{v_2^2 - v_1^2}{2l}. \tag{18}$$

Hence the total inertial force acting on the fluid is

$$\pi \bar{R}^{*2} l \rho \left(\frac{d\bar{v}}{dt} + \frac{v_2^2 - v_1^2}{2l} \right). \tag{19}$$

The applied force consists of two components: the force due to the pressure gradient, and the force due to friction. The pressure difference is $p_1 - p_2$ and the total force is

$$\pi \bar{R}^{*2}(p_1 - p_2). \tag{20}$$

To compute the force of viscous resistance, we proceed as follows:

The actual axial velocity varies from the axis to the wall, being zero at the latter. The locus of the average velocity $\bar{v}$ is somewhere halfway between axis and wall. Hence the average radial gradient of velocity is approximately $2\bar{v}/\bar{R}^*$. This produces a force per unit surface equal to $2\eta\bar{v}/\bar{R}^*$, η being the viscosity. The surface along which this shearing force acts is $4\,\pi\,\bar{R}^*\,l$. Hence the total force of resistance is equal to

$$-8\,\pi\,\eta\,l\,\bar{v}\,. \tag{21}$$

Putting the inertial force (19) equal to the sum of expressions (20) and (21), we find

$$\rho\,l\frac{d\bar{v}}{dt} + \frac{\rho(v_2^2 - v_1^2)}{2} = p_1 - p_2 - \frac{8\,\eta\,l\,\bar{v}}{\bar{R}^{*2}}. \tag{22}$$

Introducing expressions (7) and (16) into equation (22), remembering that $v_1 = v_2$, and that in the stationary state we have

$$p_{01} - p_{02} = \frac{8\,\eta\,l\,v}{\bar{R}^{*2}}, \tag{23}$$

where v is the same as in equation (13), so that $v - \bar{v} = v - v_1 = (l/\bar{R}^*)\,(d\Delta_1/dt)$, we obtain

$$-\frac{\rho\,l^2}{\bar{R}^*}\frac{d^2\,\Delta_1}{dt^2} = (\Delta\,\rho)_1 - (\Delta\,\rho)_2 + \frac{8\,\eta\,l^2}{\bar{R}^{*3}}\frac{d\Delta_1}{dt}.$$

Combining this with equation (12), we obtain

$$\left(2\,\delta\,\rho_1 + \frac{l^2\,\rho}{\bar{R}^*}\right)\frac{d^2\,\Delta_1}{dt^2} = -\frac{2\,E\,\delta}{\bar{R}^{*2}}\Delta_1 - \frac{8\,\eta\,l^2}{\bar{R}^{*3}}\frac{d\,\Delta_1}{dt}. \tag{24}$$

This is an equation of damped harmonic oscillations. As may have been expected *a priori*, the role of the viscosity is to add only a damping term. With $\eta = 0$, and with a deformation which preserves the constancy of the volume per wave length, the system may formally be considered a conservative, since the amount of energy flowing into

the tube at one end is equal to the amount flowing out at the other. In that case, equation (24) without the damping term can be readily obtained by the Lagrangian method. The kinetic energy of the vibrating walls is per wave length

$$T_1 = 2\pi R^* \delta \rho_1 l \left(\frac{d\Delta_1}{dt} \right)^2, \tag{25}$$

the bar over R^* being omitted because now in a stationary state $R^* = \text{const}$. The kinetic energy T_2 of the liquid is, per wave length, because of equation (13):

$$\begin{aligned} T_2 &= \tfrac{1}{2}\pi R^{*2} l \rho (v_1^2 + v_2^2) \\ &= \pi R^{*2} l \rho \left[v^2 - \frac{2lv}{R^*} \frac{d\Delta_1}{dt} + \frac{l^2}{R^{*2}} \left(\frac{d\Delta_1}{dt} \right)^2 \right]. \end{aligned} \tag{26}$$

The potential energy P due to the elastic forces is obtained by remembering that during the displacement Δ_1 the average force acting on the displaced part of the wall is

$$2\pi R^* l E \delta \left(\frac{1}{R_0} - \frac{1}{R^* + \frac{1}{2}\Delta} \right).$$

Hence, per wave length:

$$\begin{aligned} P &= 2\pi R^* l E \delta \left[\left(\frac{1}{R_0} - \frac{1}{R^* - \frac{1}{2}\Delta_1} \right) \Delta_1 + \left(\frac{1}{R_0} - \frac{1}{R^* + \frac{1}{2}\Delta_2} \right) \Delta_2 \right] \\ &= -\frac{2\pi l E \delta}{R^*} \Delta_1^2. \end{aligned} \tag{27}$$

Putting $T = T_1 + T_2$, and writing

$$\frac{d}{dt} \frac{\partial T}{\partial \dot{\Delta}_1} = \frac{\partial P}{\partial \Delta_1}; \quad \dot{\Delta}_1 = \frac{d\Delta_1}{dt}; \tag{28}$$

we obtain equation (24) without the damping term.

A similar result may be obtained for $\eta = 0$ by using *exact* hydrodynamical equations for infinitesimal sinusoidal deformation of the tube. This will be shown in a subsequent paper.

Neglecting the damping term, equation (24) gives a frequency

$$\nu = \sqrt{\frac{2 E \delta}{2 \delta \rho_1 R^{*2} + l^2 \rho R^*}}. \tag{29}$$

With $R^* \lesssim 1$ cm, $\delta \sim 0.1$ cm; $\rho \sim \rho_1 \sim 1$ gm cm^{-3} and $l \sim 1$ cm, this simplifies to

$$\nu = \sqrt{\frac{2 E \delta}{l^2 \rho R^*}}, \tag{30}$$

and with $E \sim 10^5$, it gives $\nu \sim 10^2$, that is, within audible range.

It must be remarked that for $\eta = 0$ there may be *two* values of R^* for the stationary state when the tube remains cylindrical. In that case, p is constant along the tube, and, if p_0 denotes the constant pressure outside of the input, we have

$$p = p_0 - \frac{\rho v^2}{2}. \tag{31}$$

If the total flow Q of liquid through a cross-section of the tube is constant, then $v = Q/\pi \rho R^{*2}$ and therefore

$$p = p_0 - \frac{Q^2}{2 \pi^2 \rho R^{*4}}. \tag{32}$$

Equations (5) now become, since $p_{01} = p_{02} = p$:

$$p_0 - \frac{E \delta}{R_0} - \frac{Q^2}{2 \pi^2 \rho R^{*4}} + \frac{E \delta}{R^*} = 0. \tag{33}$$

For reasons discussed in connection with equation (4), $p_0 - E\delta/R_0 < 0$. Therefore, as can be seen graphically, equation (33) has two positive roots, $R^{*\prime}$ and $R^{*\prime\prime} > R^{*\prime}$. Since the left side of equation (33) represents the total force acting radially upon the tube, it is also seen that $R^{*\prime\prime}$ is stable, while $R^{*\prime}$ is unstable for such deformations of the tube, which leave it a cylinder. For wave-like deformations, considered above, both may be stable. Physically, however, oscillations are not likely to occur around $R^{*\prime}$.

We do not wish to suggest that the hemic murmurs are necessarily due to such transversal vibrations of the walls of blood vessels. The experimental studies of T. Weber (1855) suggest the possibility of their being due to *longitudinal* elastic vibrations of the blood vessels. According to Weber, the mechanism may be somewhat similar to the action of a uniformly moving bow upon a violin string. Possibilities of relaxation oscillations must be definitely considered in this

connection, and further theoretical studies are indicated, of which this is only the first step.

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A PROBLEM IN THE MATHEMATICAL BIOPHYSICS OF BLOOD CIRCULATION: II. RELATION BETWEEN PRESSURE AND FLOW OF A VISCOUS FLUID IN AN ELASTIC DISTENSIBLE TUBE

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In an elastic distensible tube, like a blood vessel, the radius is determined by the equality of the hydrostatic pressure and the elastic forces. If a viscous fluid flows through such a tube, there is a pressure drop along the line of flow. This results in a variation of the radius of the tube along the axis. An approximate expression, valid within a limited range of values, is derived for the radius of the tube as a function of the distance along the axis. Another approximate expression is derived for the relation between pressure drop and total flow in such a case. For sufficiently high rates of flow the pressure drop does not vary linearly with the flow, as in the usual Poiseuille's law, but more rapidly.

In a previous paper (Rashevsky, 1945) we investigated the vibrations of the walls of an elastic tube through which a viscous fluid is flowing. We found that the frequency of those oscillations depended on the radius of the tube. But in case of a viscous liquid, that radius itself varies along the axis of the tube because it is partly determined by the hydrostatic pressure and the latter drops along the line of flow. In this paper we shall investigate the law of variation of the radius of the tube for the case of a stationary flow. The exact solution of the problem presents very great difficulties. It amounts to solving the Navier-Stokes equations for an *arbitrarily* shaped axially symmetric tube, and then determining the arbitrary function, which describes the shape, from considerations of mechanical equilibrium. We shall therefore suggest here a very crude approximation which will give us a general idea about the variation of the radius, at least within a limited range of values.

Introducing cylindrical coordinates, r, z, and ϕ, we first of all restrict ourselves to axially symmetric flows, so that ϕ and its derivatives drop out from all equations. Further, we shall restrict ourselves to the case that the radius R of the tube varies very slowly with z.

Our approximation amounts essentially to two things: first we shall neglect the very small radial component v_r of the velocity v everywhere, and second we shall assume that at each cross-section of

the tube the radial variation of the axial component v is parabolic, like in an ordinary Poiseuille flow. We shall omit the subscript z and write v for v_z. For a stationary state, when all time derivatives are zero, the Navier-Stokes system of equations reduces now to a single equation:

$$-\frac{\partial p}{\partial z}=\rho v\frac{\partial v}{\partial z}-\eta\left(\frac{\partial^2 v}{\partial r^2}+\frac{1}{r}\frac{\partial v}{\partial r}+\frac{\partial^2 v}{\partial z^2}\right), \tag{1}$$

where p denotes the pressure, ρ the density of the fluid, and η the viscosity.

Denoting by v_0 the velocity at a point of the axis, and remembering that everywhere for $r = R$, $v = 0$, we have

$$v=v_0\left(1-\frac{r^2}{R^2}\right). \tag{2}$$

The total flow Q, which in a stationary state is the same for all cross-sections, is given by

$$Q=2\pi\rho\int_0^R vrdr. \tag{3}$$

Introducing expression (2) into expression (3), we find:

$$Q=\tfrac{1}{2}\pi\rho v_0 R^2, \text{ or } v_0=\frac{2Q}{\pi\rho R^2}. \tag{4}$$

As a first approximation, we shall consider that R varies with z so slowly that the resulting variations of v with respect to z may be neglected, in other words, that we can put $\partial v/\partial z = \partial^2 v/\partial z^2 = 0$. Introducing now expressions (2) and (4) into equation (1), we find:

$$\frac{dp}{dz}=-\frac{8\eta Q}{\pi\rho R^4}, \tag{5}$$

which gives

$$p=p_0-\frac{8\eta Q}{\pi\rho}\int_0^z\frac{dz}{R^4(z)}. \tag{6}$$

Denoting by δ the thickness of the tube wall, by E its modulus of elasticity, and by R_0 the radiüs of the tube when completely unstretched, we have as the condition of mechanical equilibrium at every point [*loc. cit.* equation (5)]:

$$p - E\,\delta\left(\frac{1}{R_0} - \frac{1}{R}\right) = 0. \tag{7}$$

Introducing expression (6) into (7), we have

$$p_0 - \frac{8\,\eta\,Q}{\pi\,\rho}\int_0^z \frac{dz}{R^4(z)} - \frac{E\,\delta}{R_0} + \frac{E\,\delta}{R(z)} = 0. \tag{8}$$

Differentiating this with respect to z, rearranging and putting

$$\frac{E\,\delta\,\pi\,\rho}{8\,\eta\,Q} = A, \tag{9}$$

we obtain

$$A\frac{dR}{dz} = -\frac{1}{R^2}. \tag{10}$$

Integrated, this gives, denoting by B a constant of integration,

$$\frac{R^3}{3} = B - \frac{z}{A}, \tag{11}$$

or

$$R = \sqrt[3]{3\,B - \frac{3\,z}{A}}. \tag{12}$$

Because of the original assumption which we made about the slow variation of R with z, this expression holds only within such ranges of z for which $z/A << B$. In this case, we may expand the right side of equation (12) preserving only linear terms in z. Putting

$$\frac{1}{A\,B} = \frac{8\,\eta\,Q}{E\,\delta\,\pi\,\rho\,B} = C, \tag{13}$$

we obtain

$$R = (3B)^{1/3}\left(1 - \frac{C}{3}z\right). \tag{14}$$

The quantity $(3B)^{1/3}$ is the radius for $z = 0$, or for $p = p_0$. It is determined as the root of equation (7), into which we put $p = p_0$. Denoting that root by R_i, we have

$$R_i = \frac{E\,\delta\,R_0}{E\,\delta - p_0\,R_0}; \quad B = \frac{R_i^3}{3}; \quad C = \frac{24\,\eta\,Q}{E\,\delta\,\pi\,\rho\,R_i^3}. \tag{15}$$

Substituting expression (14) into equation (6), and making use of the second relation (15), we find after integration:

$$p_0 - p = \frac{8\eta Q}{\pi \rho R_i^4} \left(\frac{1}{C\left(1 - \frac{C}{3} z\right)^3} - \frac{1}{C} \right). \tag{16}$$

Expanding $(1 - C\,z/3)^3$, keeping only the linear terms, and using expression (15) we finally find

$$p_0 - p = \frac{8\eta}{\pi \rho R_i^4} \frac{Qz}{1 - \frac{24\eta}{E\,\delta\,\pi\,\rho\,R_i^3} Qz}. \tag{17}$$

For very small values of Q the relation between $p_0 - p$ and either Q or z is linear, as in Poiseuille's law. For larger values, however, it is not so. If R_i were constant, then $p_0 - p$ would vary more rapidly than Q or z. But R_i is itself a function of p_0. We still may keep p_0, and therefore also R_i, constant, and then see that the total flow varies more slowly with the total *drop* of pressure than in Poiseuille's law. If we, however, keep p constant and vary p_0 the situation becomes much more complicated. The flow then is not a function of the pressure difference only, but also of the absolute value of the pressure. The actual relation is obtained by substituting expression (15) for R_i into equation (17).

We may obtain a better approximation by dropping the restriction $\partial v/\partial z = 0$, but still retaining $\partial^2 v/\partial z^2 = 0$. We now introduce into equation (1) an average value $\overline{\partial v/\partial z}$, defined in the following way:

Let

$$f(z) = \frac{dR}{dz}. \tag{18}$$

Then we have

$$\frac{\partial v}{\partial z} = \frac{\partial v}{\partial R} f(z). \tag{19}$$

Introducing expression (4) into expression (2) and the latter into (19) and averaging over the whole radius R, we find

$$\overline{\frac{\partial v}{\partial z}} = \frac{8Qf(z)}{\pi \rho R^6} \int_0^R r^2 dr - \frac{4Qf(z)}{\pi \rho R^4} \int_0^R dr = -\frac{4Qf(z)}{3\,\pi\,\rho\,R^3}. \tag{20}$$

Introducing this into equation (1) and remembering that the

average value $\bar{v}$ of v is, from equations (2) and (4), equal to $\bar{v} = 4Q/\pi \rho R^2$, we now find

$$\frac{dp}{dz} = \frac{16Q^2 f(z)}{3\pi^2 \rho R^5} - \frac{8\eta Q}{\pi \rho R^4}. \tag{21}$$

Integrated, this gives

$$p = p_0 + \frac{16Q^2}{3\pi^2 \rho} \int_0^z \frac{f(z)\,dz}{R^5(z)} - \frac{8\eta Q}{\pi \rho} \int_0^z \frac{dz}{R^4(z)}. \tag{22}$$

Introducing this into equation (7), differentiating with respect to z, and rearranging, we obtain

$$\left(\frac{16Q^2}{3\pi^2 \rho} \frac{1}{R^5} - \frac{E\delta}{R^2} \right) \frac{dR}{dz} = \frac{8\eta Q}{\pi \rho} \frac{1}{R^4}. \tag{23}$$

Integrating, and denoting by C' a constant of integration, we have

$$\frac{1}{3} E\delta R^3 - \frac{16Q^2}{3\pi^2 \rho} \log R = C' - \frac{8\eta Q}{\pi \rho} z. \tag{24}$$

If we omit the second term of the left side, we obtain again the expression (11). If that term is, however, retained, we find that R is a two-valued function of z. The left side is positively infinite for $R = 0$ and for $R = \infty$, and has a minimum. Below that minimum value of R, no real values of z exist. In the neighborhood of the minimum, however, the solution is not valid since here we cannot neglect $\partial^2 v/\partial z^2$. The existence of two values of R is of the same nature as a similar phenomenon which happens for $\eta = 0$ and which has been discussed in the previous paper (Rashevsky, 1945). Only the larger value of R is stable for $\eta = 0$, and this is likely to remain true for $\eta > 0$. Sufficiently far away from the minimum, and keeping on the larger branch of R's, we again obtain equation (11) with all its consequences, for the term in R^3 prevails over the log R term in equation (24).

If we wish to obtain a still better approximation, we may drop the assumption $\partial^2 v/\partial z^2 = 0$, and introduce into equation (1) an average value $\overline{\partial^2 v/\partial z^2}$ obtained in a similar way as $\overline{\partial v/\partial z}$.

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A CONTRIBUTION TO THE MATHEMATICAL BIOPHYSICS OF VISUAL AESTHETICS

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In continuation of previous studies, inequalities between different parameters of the brain are derived which determine whether an individual prefers in general visual patterns consisting of a relatively small number of relatively strongly excited elements, or such patterns which consist of a very large number of relatively weakly excited elements. As has been discussed in a previous publication, the first type of pattern is usually represented by artificial human-made designs, whereas the second type of pattern is formed predominantly in natural landscapes and sceneries. Thus the inequalities established in this paper give us the biophysical conditions which determine an individual's preference for either artificial designs or for landscapes and other natural objects.

In preceding publications (Rashevsky, 1938b, 1940, 1942a, b; Rashevsky and Brown, 1944a, b), we have developed a biophysical theory of visual aesthetics based on the assumption that the individually felt aesthetic value of a visual pattern is proportional to the total central excitation produced by a given pattern. Applied to relatively simple artificial designs, the theory leads to predictions which are confirmed by experiment (Rashevsky and Brown, 1944a, b). It has been pointed out (Rashevsky, 1942a) that two distinct cases must be considered: one is the case of relatively few elements excited sufficiently strongly so that the thresholds of the inhibitory cross-connecting fibers may be neglected; the other is the case of a very large number of elements excited sufficiently weakly so that the inhibitory cross-connecting fibers remain unexcited. Artificial man-made designs are typical representatives of the first case, while landscapes are characteristic of the second (Rashevsky, 1942a). However, mixed cases do exist, and their occurrence is not infrequent. Thus in a landscape the aesthetic effect of the very large number of small differences in shades and hues may be just as important as the general design, or what the artist refers to as "composition". It is quite legitimate and theoretically very interesting to inquire whether a difference in the biophysical structure or biophysical parameters of the central nervous system may result in a preference by an individual towards one or another of the two types of patterns mentioned above. The problem has more than a purely theoretical inter-

est since actually different individuals display such preferences. One artist may pay much more attention to composition, another to color effects. An individual may definitely prefer a tree to a flower or vice versa. Now in a tree the geometric "design" plays a relatively subordinate role, while the effect of the very large number of different shades of green or other colors is more outstanding. Even the general outline of a tree consists of a very irregular line, with very many not too sharply defined elements. In a flower, on the contrary, the element of a geometric design is very much more pronounced.

Let us investigate the problem from the point of view of the previously developed theory. We shall use notations employed previously (Rashevsky, 1938a, Chapter xxii, referred to as *loc. cit.*; 1942a) and shall presuppose familiarity with the previous publications.

It is of course impossible to attack at present the problem in its generality. However, even some approximate, abstract, theoretical considerations are of interest. We shall therefore treat the case when all elements of a pattern are stimulated with the same intensity and all neural elements involved have the same biophysical constants.

For a "natural" pattern consisting of a large number of weakly excited elements we must always have (Rashevsky, 1938a; 1942a)

$$S_1 \leqslant h_1 + \frac{h_3}{P\,a_1\,I_1}. \tag{1}$$

If n denotes the total number of peripheral nerve fibers involved or, with our assumptions, the total number of elements, then the total central excitation is given by multiplying by n the first term of the right side of equation (53) of *loc. cit.*, since, because of expression (1), E_3, and hence the second term, are zero. Doing this and introducing expressions (10) and (61) of *loc. cit.*, we find for the total central excitation

$$E = nP\alpha_1 I_1 (S_1 - h_1). \tag{2}$$

This expression increases with n. The consequences of this have been discussed previously (Rashevsky, 1942a). For a fixed n it increases with S_1. But the latter is subject to restriction (1). Hence for a fixed n the largest possible value of E is given by

$$E_m = nh_3. \tag{3}$$

Consider now the case when

$$S_1 > h_1 + \frac{h_3}{P\,a_1\,I_1}, \tag{4}$$

so that the inhibitory cross fibers are excited. Then the total central excitation E' is obtained by multiplying by n the right side of expression (60) of *loc. cit.* This gives

$$E' = n\{P\,\alpha_1 I_1(S_1 - h_1) - (n-1)\,Q\,\alpha_3 I_3[P\alpha_1 I_1(S_1 - h_1) - h_3]\}. \tag{5}$$

For a fixed S_1, the quantity E' has a maximum for

$$n = \frac{P\,\alpha_1 I_1(S_1 - h_1) + Q\,\alpha_3 I_3[P\,\alpha_1 I_1(S_1 - h_1) - h_3]}{2\,Q\,\alpha_3 I_3[P\,\alpha_1 I_1(S_1 - h_1) - h_3]}, \tag{6}$$

and that maximum value is equal to

$$E'_m = \frac{\{P\,\alpha_1 I_1(S_1 - h_1) + Q\,\alpha_3 I_3[P\,\alpha_1 I_1(S_1 - h_1) - h_3]\}^2}{4\,Q\,\alpha_3 I_3[P\,\alpha_1 I_1(S_1 - h_1) - h_3]}. \tag{7}$$

The value of E'_m increases with S_1, and at first glance may be made infinite by taking a sufficiently large S_1, Actually this is not so. Expression (7) is derived on the assumption of a linear relation between E_1 and S_1, and such a relation holds only for not too large values of S_1. As S_1 increases, E_1 tends to its maximum values I_1/θ_1, θ_1 being the refractory period. For very large values we therefore must substitute I_1/θ_1, for $\alpha_1 I_1(S_1 - h_1)$ into equation (7), and thus obtain

$$E'_m = \frac{\{P\,I_1/\theta_1 + Q\,\alpha_3 I_3[P\,I_1/\theta_1 - h_3]\}^2}{4\,Q\,\alpha_3 I_3[P\,I_1/\theta_1 - h_3]}. \tag{8}$$

Equation (8) holds still subject to the assumption that while the excitatory fibers have reached their saturation values of excitation, the inhibitory fibers are still within the linear range. If the latter are also near their saturation, we have, instead of equation (8),

$$E'_m = \frac{[P\,I_1/\theta_1 + Q\,I_3/\theta_3]^2}{4\,Q\,I_3/\theta_3}. \tag{9}$$

Finally the case must be considered when the inhibitory fibers reach their saturation, while the excitatory are still in the linear range. We then have

$$E'_m = \frac{[P\,\alpha_1 I_1(S_1 - K) + Q\,I_3/\theta_3]^2}{4\,Q\,I_3/\theta_3}. \tag{10}$$

In this case again E'_m increases with S_1, and its maximum value is

reached when E_1 becomes equal to I_1/θ_1. Then equation (10) reduces to equation (9).

If E'_m is approximately equal to E_m, then the individual has no particular preference for either "natural" or "artificial" patterns. If $E'_m >> E_m$, the individual prefers artificial designs; if $E'_m << E_m$, the person prefers "natural" patterns. Since the maximum possible value n_m of n in equation (3) is a constant for a given individual, the above inequalities give us the relations we are looking for. In case of equation (8) the condition for preference of geometric designs is given by

$$\frac{\{P I_1/\theta_1 + Q \alpha_3 I_3[P I_1/\theta_1 - h_3]\}^2}{4 Q \alpha_3 I_3[P I_1/\theta_1 - h_3]} >> n_m h_3. \tag{11}$$

In case of equation (9) we have

$$\frac{[P I_1/\theta_1 + Q I_3/\theta_3]^2}{4 Q I_3/\theta_3} >> n_m h_3. \tag{12}$$

In both cases low threshold h_3 of inhibitory fibers favors preference for geometric designs. For a fixed h_3 a large n_m, which may be interpreted as a more developed central nervous system, favors preference for "natural" patterns. For very large I_3 inequality (12) becomes

$$\frac{Q I_3}{4 \theta_3} >> n_m h_3, \tag{13}$$

indicating that very strong inhibitory fibers favor preference for geometric designs.

For a fixed value of I_1/θ_1, the left side of inequality (12) has a minimum for

$$\frac{I_3}{\theta_3} = \frac{P}{Q}\frac{I_1}{\theta_1}, \tag{14}$$

the value of that maximum being $P I_1/\theta_1$.

If

$$P I_1/\theta_1 > n_m h_3, \tag{15}$$

then for values of I_3/θ_3 which are sufficiently smaller or larger than those given by equation (14), inequality (12) will be always satisfied, the individual prefering geometric designs. Even if inequality (15) does not hold, inequality (12) holds for sufficiently small or sufficiently large values of I_3/θ_3, since the left side of equation (12) is

infinite for $I_3/\theta_3 = 0$ and for $I_3/\theta_3 = \infty$. But in general, $P/Q \approx 1$. Hence equation (14) implies $I_3/\theta_3 \approx I_1/\theta_1$. In other words, an individual with either too weak or too strong inhibitory neurons will prefer geometric designs. For the preference of "natural" patterns or for lack of definite preference, the saturation excitations of excitatory and inhibitory fibers must be approximately equal.

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